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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/612,921 07/10/00 SIMS

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EXAMINER

HM22/0730

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PRASAD S  
ART UNIT PAPER NUMBER

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

<b>Office Action Summary</b>	Application No.	Applicant(s)	
	09/612,921	Sims, John E.	
	Examiner	Art Unit	
	Sarada C Prasad	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 09 April 2001.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 13-41 is/are pending in the application.
- 4a) Of the above claim(s) 16-21, 25-34 and 36-41 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 13-15, 22-24 and 35 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

- |   |  |
|---|--|
| 15) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 18) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 16) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 19) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 17) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>4</u> | 20) <input type="checkbox"/> Other:  |

***Detailed Action***

1. Applicants' election with traverse of Group I (claims 13-15, 22-24, and 35 directed to SEQ ID NO: 3 and 4) in Paper No. 7 (4/9/01) is acknowledged. The traversal argument is on the grounds that searching SEQ ID Nos: 1-4 would not be a burden to the examiner because they encode for homologous polypeptides of different species. However, this argument is not found persuasive because searching for more than one SEQ ID No. per application would be a burden on the office. However, in the instant case the polypeptide and polynucleotide of a single species would be searched to examine the elected claims with respect to one species, i.e., SEQ ID Nos. 3 and SEQ ID No. 4 representing human homologues. Therefore, currently, claims 13-15, 22-24, and 35 are under consideration with respect to SEQ ID Nos. 3 and 4.

***Specification***

2. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

***Claim Rejections - 35 USC § 101***

3. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 13-15, 22-24, and 35 are rejected under 35 USC § 101 because they are drawn to an invention with no apparent or disclosed utility.

The instant application has provided a description of a human interleukin-delta (IL-1 delta), nucleic acids encoding it, methods of expression, possible uses of the polynucleotides and polypeptides as well as their biological activities. The breadth of its possible uses have been disclosed in the specification, and they are largely dependent upon the structural homology of the

instant IL-1 delta to mature forms of the other human IL-1 family members (see specification, page 9, 6<sup>th</sup> para, lines 1-5). In fact the identities were 29% with IL-1 $\beta$ , 50% with IL-1ra, 31% with IL-1 epsilon, and 34% with IL-1 zeta, and no identity with IL-1 $\alpha$  and IL-18.

The instant invention lacks patentable utility because the phenomena of the ligand IL-1 delta binding to its receptor and transduction of the signal for the claimed effectiveness and functionality of the IL-1 delta are hypothetical. It is clear from the instant specification that the protein IL-1 delta of SEQ ID No. 3 is a homologue of certain forms of IL-1. In fact, instant specification discloses (page 10, 2<sup>nd</sup> para, lines 1-3) that a soluble version of the IL-1 delta receptor may act as an antagonist of other active cytokines, in the same way as that IL-1ra is an antagonist of the actions of IL-1 $\alpha$  and IL-1 $\beta$ . Such explanation is certainly based on assumption that based on homology it would be useful as an antagonist or agonist of the other forms of IL-1. There is little doubt that, after further characterization, this protein will probably be found to have a patentable utility. This further characterization, however, is part of the act of invention and until it has been undertaken, and Applicant's claim of its utility as a novel cytokine is incomplete.

The instant situation is analogous to that which was addressed in *Brenner v Manson*, 148 USPQ 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which are known to possess anticancer activity was alleged to be a potential antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 USC 101, which requires that an invention

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must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

"The basic quid pro contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-here is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and a "patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion".

The instant claims are drawn to polynucleotides and polypeptides which exhibit homology to various forms of IL-1, however, as of yet not shown to have their own identity by way of demonstrated biological effects or functions. Until some actual and specific significance can be attributed to the proteins identified in the specification as SEQ ID NO. 4 and proteins encoded by SEQ No. 3, the instant invention is incomplete. In the absence of knowledge of the biological significance of these proteins, there are no immediately obvious patentable uses for these IL-1-like homologues. Since the instant invention does not disclose a "real world" use for proteins of SEQ ID NO. 4, the claimed invention is incomplete, and therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claims 13-15, 22-24, and 35 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

***Claim Rejections - 35 USC § 112-First paragraph***

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4a. Claims 13-15, 22-24, and 35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid molecule that encodes a polypeptide comprising SEQ ID No. 4, a nucleic acid molecule of SEQ ID No. 3, does not reasonably provide enablement for a nucleic acid molecule that encodes a fragment of the polypeptide of SEQ ID No. 4, wherein the 'fragment binds to an IL-4 delta counterstructure', and 'a nucleic acid molecule that hybridizes to either strand of a denatured, double stranded DA comprising the nucleic acid encoding SEQ ID No. 4'. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 13, sub-parts (b)-(c) and claim 22 recite 'a nucleic acid molecule that encodes a fragment of the polypeptide of SEQ ID No. 4, wherein the fragment binds to an IL-1delta counterstructure'. The claim language reads on 'molecules that fragments of IL-1delta could bind to' the chemical nature of which is not recited in the claim. State of the art suggests that cytokines such as IL-1 delta bind to receptor to transduce signal and mediate cellular responses. However, one of skill in the art would not know what are the counterstructure molecules and what is included or what is excluded from the list of such counterstructure molecules. Therefore, knowledge of the polynucleotide sequence encoding a homologue, and the encoded polypeptides does not allow, one skilled in the art, to envision and make the fragments of any desired length that possess the desired properties, for example, can bind to counterstructure molecules. Predictability in the art requires the fragment length, starting and ending amino acids that bind to the counter structure molecules. Without guidance in the specification, it requires undue experimentation, for one of skill in the art, to practice the invention as claimed.

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Therefore, the instant specification is non-enabling for practice of claims 13-15, 22-24, and 35.

4b. Claim 13, sub-part (c) recites 'nucleic acid molecule that hybridizes to either strand of a denatured, double stranded DNA.....'. The claim language reads on muteins of the instant polypeptides represented by SEQ ID No. 4 and variants of the nucleic acid that encodes the polypeptide of SEQ ID No. 4. The specification is enabled for making polypeptides of SEQ ID No. 4 and also a nucleic acid molecule of SEQ ID No. 3 that could encode for IL-1 delta polypeptides. However, the specification is non-enabling for variants or muteins of the polypeptides that could be encoded by the nucleic acids envisioned by sub-part (c) claim 13. No guidance is provided in the specification as to how one of skill in the art should be selecting the polypeptide variants, and hence the nucleic acids encoding such variants based on the hybridization language of the sub-part (c) of claim 13. It requires undue experimentation to select all possible variants and test to find out if they would bind to IL-1 delta receptor, or compete with the wild type IL-1 to bind to the receptor.


4c. Claims 22-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide of SEQ ID No. 4, does not reasonably provide enablement for 'a polypeptide that comprises an amino acid sequence that is at least 80% identical to SEQ ID No. 4'. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claim 22 is overly broad in reciting 'a polypeptide that comprises an amino acid sequence that is at least 80% identical to SEQ ID No. 4'. The claim language reads on variants

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of polypeptides represented by SEQ ID No. 4. The specification is non-enabling for a myriad of variants for which no guidance is provided. The specification has not described as to which of the several polypeptide species encompassed by the claims will represent a polypeptide which retains the activity of IL-1delta. Applicants disclose that variants can be generated without disclosing any actual or prophetic examples on the expected outcome or performance characteristics of any of the possible muteins of the instant polypeptide. However, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation inhibition factor (GIF) protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino acid change in a protein's sequence can dramatically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and pages 230, column 2, first paragraph).

There is no guidance provided in the instant specification as to how one of skill in the art would generate a polynucleotide encoding a T1 receptor like ligand other than that exemplified in the specification. The test of enablement is not whether any experimentation is necessary, but





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whether, if experimentation is necessary, is it undue (*In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404). Therefore, considering the breadth of claim 22, state-of-the-art, guidance provided in the specification, the amount of experimentation required is undue to practice the invention as claimed.

Claims 23, 24 are rejected insofar as they depend on claim 22.

4d. Claims 22-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 22 recites 'a nucleic acid molecule that encodes a polypeptide that comprises an amino acid sequence that is at least 80% identical to SEQ ID No. 4...'. The written description in this case sets forth the polynucleotide of SEQ ID No. 3 and the encoded polypeptide of SEQ ID No. 4 corresponding to IL-1 delta. However, written description is not commensurate with claim drawn to a polypeptide 'at least 80% identical to SEQ ID No. 4...'. Specification describes general methods of recombinant expression of polypeptides, and their use in detecting such polypeptides in biological samples. However, there is no actual reduction to practice of the claimed invention, or expression of the said polypeptides with at least 80% identity to the SEQ ID No. 4, or measurement/detection of expected signal transduction, or recognition of the specific polypeptides of SEQ ID No. 4, or polypeptides encoded by SEQ ID No. 3 by cognate receptors, either in the examples, or in specification.

Conception of the claimed invention can not be achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the potential methods for expressing the

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protein, by recombinant methods. Therefore the Applicants have not provided sufficient evidence that they were in possession of the invention at the time of filing as it is claimed and thus written description requirement has not been satisfied for the claims as they are recited.

Applicant's attention is drawn to Guidelines for the examination of patent Applications under 35 U.S.C. 112 first paragraph, "Written Description" requirement, federal register, Vol.66, No. pages 1099-111, Friday, January, 2001.

Therefore claims 13-15, 22-24, and 35 are rejected under 35 USC 112 first paragraph as lacking an adequate written description.

***Claim Rejections - 35 USC § 112-Second Paragraph***

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 13 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 13 and 22 recite '...the fragment binds to an IL-1 delta counterstructure'. It is not clear as to what is meant by the phrase 'counterstructure' that binds to a polypeptide fragment. Is it antagonist or agonist and what is the property that is guiding such binding? This rejection can be obviated by reciting the conventional way of referencing the meaning of counterstructure.

Claims 14-15, 23-24, and 35 are rejected insofar as they depend on claims 13 and 22.

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***Conclusion***

6. No claims are allowed.

***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sarada C Prasad whose telephone number is 703-305-1009. The examiner can normally be reached Monday - Friday from 8.00 AM to 4.30 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Sarada Prasad, Ph.D.  
Examiner  
Art Unit 1646  
July 17th, 2001

*Prema Mertz*  
**PREMA MERTZ**  
**PRIMARY EXAMINER**